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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,975	02/21/2002	Kar Wai C. Tao	3790-62404	9952

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EXAMINER	
FLOOD, MICHELE C	
ART UNIT	**PAPER NUMBER**
1654	

DATE MAILED: 06/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,975	C. TAO ET AL.	
	Examiner	Art Unit	
	Michele C. Flood	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 February 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *9-13,15,19-21,24-31 and 33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,14,16-18,22,23,32,34 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgment is made of the receipt and entry of the amendment filed on February 20, 2004, and newly added Claims 34 and 35.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-8, 14, 16-18, 22, 23, 32, 34 and 35 are under examination.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Newly added Claim 35 is rejected under 35 U.S.C. § 112, first paragraph, as failing to provide prior support or antecedent basis for the language "wherein the composition does not include a surfactant". Newly applied as necessitated by amendment.

The newly submitted claim as set forth in the amendment filed February 20, 2004, now recites an oral dosage composition of a high molecular weight, lipophilic, bioactive agent comprising: a biologically effective amount of the bioactive agent; a lipid matrix in which the bioactive agent is suspended; and a sufficient amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered, wherein the composition does not include a surfactant.

However, the specification as originally filed provides only for compositions comprising an oral dosage composition of a high molecular weight, lipophilic, bioactive agent, comprising: a biologically effective amount of the bioactive agent; a lipid matrix in which the bioactive agent is suspended; and a sufficient amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered, wherein the lipid matrix comprises a triglycerides matrix that is liquid at body temperature, wherein the triglyceride matrix comprises a soybean lipid matrix; and, wherein the lipid matrix comprises a mixture of refined soybean oil; mono-, di- and triglycerides, and polyglycerol oleate and/or polyglycerol dioleate.

Insertion of the above mentioned claim limitation has no support in the as-filed specification. The insertion of the limitation is a new concept because it neither has literal support in the as-filed specification by way of generic disclosure, nor are there specific examples of the newly limited genus which would show possession of the concept of the claim-designated composition, especially in view of the fact that both polyglycerol oleate and polyglycerol dioleate are known in the art of chemistry as surfactants. There is only one exemplified an oral dosage composition of a high molecular weight, lipophilic, bioactive agent comprising an effective amount of a biologically active agent; a lipid matrix in which the bioactive is suspended, which inherently comprises surfactants, namely polyglycerol oleate and/or polyglycerol dioleate; and a sufficient amount of a polyphenol to improve the gastrointestinal absorption of the bioactive agent when the oral dosage is orally administered. This is not sufficient support for the new genus of "An oral dosage composition of a high molecular weight, lipophilic, bioactive agent comprising: a biologically effective amount of the bioactive agent; a lipid matrix in which the bioactive agent is suspended; and a

sufficient amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered, wherein the composition does not include a surfactant." This is a matter of written description, not a question of what one of skill in the art would or would not have known. The material within the four corners of the as-filed specification must lead to the generic concept. If it does not, the material is new matter. Declarations and new references cannot demonstrate the possession of a concept after the fact. Thus, the insertion of the above mentioned claim limitation is considered to be the insertion of new matter for the above reasons.

As the above mentioned claim limitation could not be found in the present specification, the recitation of the claim limitation is deemed new matter; and, therefore it must be omitted from the claim language, unless Applicant can particularly point to the specification for literal support.

Claim Rejections - 35 USC § 102

Claims 1-8, 14, 22, as amended, and newly added Claim 34 remain/is rejected under 35 U.S.C. 102(a) as being anticipated by Chopra (N) and Claims 1-8, 14, 22, as amended, and newly added Claim 34 remain/is rejected under 35 U.S.C. 102(e) as being anticipated by Chopra (A), as evidenced by the teachings of Fox et al. (B, used herein only to establish that polyglycerol oleate and polyglycerol dioleate are surfactants). The rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant claims an oral dosage composition of a high molecular weight, lipophilic, bioactive agent consisting essentially of: a biologically effective amount of the bioactive agent; a lipid matrix in which the bioactive agent is suspended; and a sufficient

amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered.

Applicant argues that the Chopra publications disclose a composition that requires a surfactant whereas the composition instantly claimed by Applicant does not contain a surfactant. Applicant further argues that the specification discloses that inclusion of a surfactant (in the making of the claimed composition) could cause side-effects in subjects consuming the composition, such as diarrhea. Thus, Applicant concludes that amendment of the preamble overcomes the teachings of Chopra. However, Applicant's arguments are not persuasive because the composition instantly disclosed by Applicant comprises surfactants, *i.e.,* polyglycerol oleate and/or polyglycerol dioleate, as evidenced by the teachings of Fox. *See* patent claims. Thus, each of the references of Chopra are deemed to teach the claimed invention because Chopra (A, referred herein for convenience as both A and N contain the same subject matter) teaches a composition comprising a biologically effective amount of a high molecular weight, lipophilic, bioactive agent, *i.e.*, Coenzyme Q or Coenzyme Q in its reduced form (ubiquinone) in an amount ranging from 0.5%-15% or 1% to about 10% (*see* Column 1, line 64 to Column 2, line 4); a lipid matrix in which the bioactive agent is suspended, *i.e.*, vegetable oil or a triglyceride or a phospholipid derived from soy or egg (*see* Column 2, lines 7-14; Column 4, line 21 to Column 5, line 31; and, Column 6, line 64 to Column 7, line 41), wherein the amount of triglyceride ranged from about 0.1% to about 35% by weight of the composition and wherein the amount of phospholipid ranged from about 0% to about 25%, preferably about 1.0% to about 15% by weight of

the composition; and a sufficient amount of a polyphenol to improve gastrointestinal absorption of the bioactive agent when the dosage is orally administered, *i.e.*, resveratrol, grape seed extract, flavonoids, *etc.* (*see* Column 6, line 42 to Column 7, line 8), wherein the amount of the polyphenol ranged from 0.1% to about 20%, more preferably about 0.01% to about 25% by weight of the composition (*see* Column 8, lines 1-5). *See* Claims (especially, Claims 10-15, 18, 20-3, 26-28, and 30-32).

Although Chopra does not expressly teach that the polyphenol comprising his composition improves gastrointestinal absorption of the bioactive agent when the dosage form is orally administered, the ingredients comprising the composition taught by Chopra are one and the same as the ingredients comprising the composition claimed by Applicant, and the amounts of the ingredients thereof are one and the same as claimed by Applicant. Therefore, the functional effect of the polyphenol comprising the composition taught by Chopra is inherent to the composition taught by Chopra.

It is noted that the claims now recite the administered composition as one "consisting essentially of 'the claim-designated ingredients'. It is also noted that the composition disclosed in the cited prior art contains ingredients in addition to the bioactive agent, lipid matrix, and polyphenol recited in independent Claim 1. MPEP § 2111.03 clearly states that "[t]he transitional phrase 'consisting essentially of' limits the scope of a claim to the specified materials or step 'and those that do not materially affect the basic and novel characteristic(s)' of the claimed invention." (Citations omitted, emphasis in original). Moreover, MPEP § 2111.03 states that claims recited in "consisting essentially of" language should be construed as if recited in open

"comprising" language, absent some evidence that the additional ingredients in the prior art process/product materially affect the basic novel properties of the claimed invention, particularly in view of the fact that the compositions disclose by Applicant comprise surfactants:

For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., *PPG [Industries v. Guardian Industries],* 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase 'consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also *In re Janakirama-Rao*, 317 F.2d 951, 954, 137 USPQ 893, 895-96 (CCPA 1936).

On the current record there is no evidence that any of the additional ingredients present in the prior art composition would affect the basic and novel properties of the prior art composition such that the prior art composition is truly different than the claimed composition. Thus, Applicant's claims must be construed as if reciting "comprising" language, thereby encompassing the additional ingredients in the prior art composition, despite the "consisting essentially of" language. A holding of anticipation/obvious is therefore required.

Lastly, note specifically that MPEP § 2111.03 further provides that "[w]hen an applicant contends that additional steps or materials in the prior art are excluded by the

recitation of 'consisting essentially of,' applicant has the burden of showing that the introduction of additional steps or components would materially change the characteristics of applicant's invention." (Citations omitted.)

Each of the references of Chopra (A and N) anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

Claims 1-8, 14, 16-18, 22, 23 and 32, as amended, and newly added claim 34 remain/is rejected under 35 U.S.C. 103(a) as being unpatentable over Chopra (A or N) in view of Chopra (A or N) and prior art readily admitted by Applicant. The rejection stands for the reasons set forth in the previous Office action and for the reasons set forth below.

Applicant's arguments have been fully considered but they are not deemed persuasive because the cited references provide the suggestions and motivation to the claimed invention.

Applicant's main argument is directed to the idea that there is no suggestion or motivation in the Chopra' references to exclude surfactants to make the instantly claimed compositions. Applicant further argues that the compositions taught by Chopra require a surfactant to "promote the solubility of the ubiquinone." Applicant further argues that the composition disclosed by Applicant excludes surfactants, whereas the composition disclosed by the Chopra publications require a surfactant for its utility. However, Applicant's arguments are not persuasive for the reasons clearly set forth in

the rejections made under 35 USC 112, first paragraph, and the rejections made under 35 USC 102 because although Applicant argues that the instantly claimed invention excludes surfactants, it is quite apparent that the disclosed lipid matrices, as exemplified by the disclosed Gel Oil SC [comprised of refined soybean oil, mono-, di and/or triglycerides, polyglycerol oleate and/or dioleate] in Tables 4-6 on pages 22-23 comprise surfactants. Thus, the teachings of Chopra were relied upon for the reasons set forth in the previous Office action and for the reasons set forth in the rejections made under 35 U.S.C. 112, first paragraph and 35 U.S.C. 102 set forth immediately above. Therefore, although Chopra does not expressly teach a composition further comprising an antioxidant other than the bioactive agent and polyphenol, wherein the composition further comprises 2-3% of an antioxidant other than the bioactive agent and polyphenol, and wherein the antioxidant comprises a pharmaceutically acceptable salt or ester of the antioxidant, it would have been obvious to one of ordinary skill in the art at the time the invention was made to add the instantly claimed ingredients in the instantly claimed amounts to the composition taught by Chopra to provide the claimed composition because, in Column 9, lines 20-36, Chopra teaches adding ubiquinone to a premixed solution of triglyceride (and optionally, vitamin E or a vitamin E ester), and adding additional bioactive agents. At the time the invention was made, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to add an amount of an additional antioxidant other than the bioactive agent and the polyphenol comprising the composition taught by Chopra (such as, those ingredients recited in the Markush of Claim 18) to provide the claimed invention

because Chopra teaches that the active components of his composition can be mixed with other active materials, which do not adversely impair their [therapeutic] action, *e.g.*, Vitamin E (tocopherol) and esters thereof, alpha-lipoic acid, *etc.*, in Column 9, lines 54-63. Moreover, it also would have been obvious to one of ordinary skill in the art to optimize the referenced composition by adjusting the amount of antioxidant ingredients taught by Chopra to provide the claimed composition because Chopra suggests that any amount of any other active ingredient can be added in the making of his composition, as long as the active ingredient does not unfavorably affect the effect of the other components comprising the referenced composition. At the time the invention was made, one of ordinary skill in the art would have been motivated and one would have had a reasonable expectation of success to optimize the Chopra' composition by adjusting the amount of antioxidant comprising the composition taught by Chopra to the instantly claimed percentage amount to provide the claimed invention because Chopra teaches, in Column 7, lines 8-48 and Column 9, lines 20-63, the amounts of additional antioxidants which can be used in the making of the referenced composition and teaches that such ingredients provide therapeutic beneficial effects when administered to patients for various treatments. Thus, the effective varying of the amounts of the antioxidants taught by Chopra would have been no more than a routine matter of optimization for one of ordinary skill in the art at the time the invention was made.

Applicant continues to argue that the publications of Chopra teach against the exclusion of surfactants, whereas "Applicants' composition includes a polyphenol because Applicants discovered that 'polyphenolic compounds can increase the

absorption of a large, high molecular weight, orally ingested, lipophilic bioactive agent or combination of bioactive agents when these materials are administered from a triglyceride matrix." However, Applicant's argument is not persuasive because Applicant readily admits that the crux of the claimed invention depends on the administration of a large, high molecular weight, orally ingested, lipophilic bioactive agent or combination of bioactive agents co-administered from a triglyceride matrix, which inherently comprise one and the same oils and surfactants, as disclosed by Applicant, that improve the solubility of the bioactive agent ubiquinone and enhance bioavailability and dissolution of the bioactive agent when formulated into oral dosage compositions, and which can combine with other bioactive agents, such as polyphenols, that Chopra expressly teaches supplements the desired activity of the included material.

With regard to Applicant's argument that "the composition in the Chopra publications only optionally include an active agent (column 2, line 19) which may include resveratrol (column 6, lines 42-65), Applicant is directed to the patent claims wherein Chopra (A) clearly claims an oral composition in combination with an amount of a secondary bioactive other than ubiquinone, *e.g.*, resveratrol, pine bark extract (proanthocyanidins), grape seed extract, bilberry extract, flavonoids, *etc.*; a triglycerides, and a phospholipid. Although Applicant argues that the secondary bioactive polyphenols are an optional ingredient comprising the compositions taught by Chopra, the patent claims clearly disclose the claimed invention. Finally, with regard to Applicant's argument that one of ordinary skill in the art would not have found it obvious to exclude the surfactant from the composition disclosed by Chopra and instead use a

polyphenolic compound to increase bioavailability of a bioactive agent, the Office notes that Chopra expressly teaches the amounts of the ingredients comprising the reference oral composition depend on the concentration of ubiquinone in the composition. *See* Column 11, lines 21-38; *See* Column 3, linen1-67, wherein Chopra teaches that the use of surfactants are used to promote solubility of ubiquinone and that the use of Span 80 in formulating the reference composition may be optional; *See* Column 4, line 59 to Column 5, line 31, wherein the reference phospholipids comprising the reference composition promote ubiquinone solubility; *See* Column 5, line 64 to Column 6, line 41, wherein Chopra teaches triglycerides comprising the reference composition serve as a solubilizer or compartibilizer to promote uniformity of the composition; and, *See* Column 6, line 43 to Column 7, line 8, wherein Chopra teaches that the bioactive agent in addition to ubiquinone comprising the reference composition, especially lipid soluble components, may be used to enhance solubility of ubiquonine. Thus, contrary to Applicant's arguments and given the state of the art as readily admitted by Applicant that amounts of surfactants comprising oral dosage compositions for the delivery of therapeutic bioactive agents may induce undesirable side-effects to patients receiving such compositions, at the time the invention was made it would have been obvious to one of ordinary skill in the art, and would have been motivated and one would have had a reasonable expectation of success to provide the instantly claimed composition by combining the instantly claimed ingredients and minimizing the surfactants comprising the oral compositions taught by Chopra because Chopra teaches that the varying of the amounts of the ingredients comprising his invention depend upon a result effect variable

relative to the solubility, dissolution, and enhancement of the bioavailability of the high molecular weight, lipophilic bioactive agent of ubiquinone comprising the reference oral dosage composition; and, considering that the inclusion of surfactants in oral compositions to deliver therapeutic bioactive agent may induce unwanted side effects, such as diarrhea as readily admitted by Applicant. Hence, as each of the references and the readily admitted prior art clearly indicate that the various proportions and amounts of the ingredients used in the claimed composition combination are result variables, they would have been routinely optimized by one of ordinary skill in the art practicing the invention disclosed by the reference. Therefore, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, especially in the absence of evidence to the contrary.

No claims are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele C. Flood whose telephone number is (571) 272-0964. The examiner can normally be reached on 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on (571) 272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

MCF
May 29, 2004

CHRISTOPHER R. TATE
PRIMARY EXAMINER